ORIGINAL RESEARCH

Intramuscular lesions in musculoskeletal MRI as a favourable prognostic sign in patients with anti-MDA5 antibody-positive dermatomyositis

Yohsuke Oto, Ken Yoshida, Takeshi Fukuda, Taiki Fukuda, Taro Ukichi, Kentaro Noda, Haruyasu Ito, Daitaro Kurosaka

ABSTRACT

Objectives Anti-differentiation-associated gene 5 (MDA5) antibody-positive dermatomyositis, which has been described as clinically amyopathic dermatomyositis, complicates rapidly progressive interstitial lung disease (ILD). Owing to the absence of significant muscle symptoms, musculoskeletal MRI is often not performed. In this study, we aimed to devise a simple evaluation method using musculoskeletal MRI findings to elucidate the relationship between MRI findings and ILD prognosis and development.

Methods The medical records and MRI scans of the proximal muscles at the time of diagnosis were retrospectively reviewed for 28 patients with anti-MDA5 antibody-positive dermatomyositis who were admitted to The Jikei University Hospital and The Jikei University Kashiwa Hospital between January 2008 and March 2022. Three observers evaluated nine proximal muscles for high signals on either short-tau inversion recovery images and/or fat-saturated gadolinium-enhanced T1-weighted images in the fascia and/or in the margins of the muscles in contact with the fascia (fascial pattern), and/or high signals in the muscles away from the fascia (intra muscular pattern), and a consensus was reached.

Results Of the 28 patients, 15 presented with ‘radiological myositis’, where an intramuscular pattern was observed at any site. Patients with radiological myositis had significantly higher survival rates than those without radiological myositis, despite the lower rate of triple therapy with prednisolone, calcineurin inhibitors and cyclophosphamide. The spread of ILD on chest CT negatively and significantly correlated with the proportion of intramuscular lesions.

Conclusion The detection of intramuscular lesions on musculoskeletal MRI using our novel evaluation method could be clinically useful as a favourable prognostic marker.

INTRODUCTION

In patients with dermatomyositis (DM), the presence of anti-differentiation-associated gene 5 (MDA5) antibodies is associated with an increased risk of complicating treatment-resistant and fatal rapidly progressive interstitial lung disease (RP-ILD). Although the survival rate in anti-MDA5 antibody-positive DM has increased after the administration of the triple therapy with high-dose prednisolone, calcineurin inhibitors and cyclophosphamide, relative to earlier treatments, immunosuppressive therapy-associated infections are clinically challenging. Intensive immunosuppressive therapy should be
administered to patients with poor prognoses but avoided in those with favourable prognoses.

Recently, it has been reported that anti-MDA5 antibody-positive DM may be divided into multiple phenotypes based on different prognoses based on age, sex, clinical symptoms and laboratory findings. Additionally, patients with muscle weakness may have good prognoses for RP-ILD. Although measuring muscle weakness is one method of evaluating muscle lesions, this method has poor objectivity and reproducibility. This issue arises as a result of confounding factors, such as muscle pain due to fasciitis, patient fatigue, joint pain and interobserver variability, which may affect the results. By contrast, musculoskeletal MRI is a more objective method for evaluating muscle lesions.

Before a specific autoantibody was identified, anti-MDA5 antibody-positive DM was widely known as ‘clinically amyopathic DM’, which is characterised by limited muscle symptoms and the typical skin manifestations of DM. As RP-ILD, not myopathy, is the major clinical issue in these patients, muscle lesions have not been analysed using MRI. Furthermore, the relationship between MRI findings and the prognosis of ILD remains unclear.

We previously focused on fascial lesions in DM and reported that both the muscle and fascia are major target sites. Additionally, each type of idiopathic inflammatory myopathy (IIM) was characterised by MRI findings when analysing the subcutaneous, fascial and distribution patterns of intramuscular lesions.

Thus, we developed a novel method to evaluate muscle lesions on MRI that separately evaluates fascial lesions and intramuscular lesions of the upper and lower proximal muscles. Using this novel method, we retrospectively analysed 28 patients with anti-MDA5 antibody-positive DM. This observational study aimed to evaluate whether musculoskeletal MRI findings can predict prognosis and if the myositis findings on MRI are associated with ILD.

METHDS
Study design
We retrospectively reviewed the medical records of adult patients with anti-MDA5 antibody-positive DM, who were admitted to the Division of Rheumatology at The Jikei University Hospital (Tokyo, Japan) between January 2008 and March 2022 as well as those admitted to the Department of Internal Medicine of The Jikei University Kashiwa Hospital (Chiba, Japan) between April 2019 and March 2022 and who received treatment from the Division of Rheumatology. To identify eligible patients, we applied the ‘probable or definite IIM’ criteria. We defined muscle weakness as a score of ≤4 on a 5-point manual muscle testing (MMT) scale or a score of ≤9 on a 10-point MMT scale in these criteria. From the selected group, we specifically focused on individuals who tested positive for anti-MDA5 antibodies. In addition, we included patients who underwent chest CT and MRI of either the thigh muscles, right upper arm or left upper arm at the time of diagnosis. Images taken more than 10 days after initial treatment were excluded.

Laboratory findings
Anti-MDA5 antibody levels were measured using an in-house ELISA at Keio University prior to 2016, and a commercial ELISA kit (SRL, Tokyo, Japan and BML, Tokyo, Japan) from 2017 onwards. The risk scores, a mortality prediction model proposed by Gono et al in PM/DM-ILD, were calculated from the number of risk factors: serum C reactive protein (CRP; ≥0.8 mg/dL) and Krebs von den Lungen-6 (KL-6; ≥1000 U/mL). In patients with anti-MDA5 antibody-positive, a score of 0 corresponds to a low risk of mortality (<15%), a score of 1 indicates a moderate risk (15%–50%) and a score of 2 indicates a high risk (≥50%).

Imaging
MRI protocol
Muscles in the upper arms and/or thighs were evaluated by MRI using a 1.5T unit (MAGNETOM Symphony or Avanto; Siemens Healthineer, Erlangen, Germany) and 3.0T unit (MAGNETOM Skyra or Vida; Siemens Healthineer, Erlangen, Germany) following a standardised protocol. The left and right thighs were imaged simultaneously, whereas the left and right upper arms were imaged separately. Short-tau inversion recovery (STIR) imaging and fat-saturated (FS) Gd-T1-weighted imaging (T1WI) were performed in the axial and coronal planes. The contrast agents used in this study, namely, gadopentetate dimeglumine (Magnevist; Bayer Yakuhin, Osaka, Japan), gadodiamide (Omniscan; Daiichi Sankyo, Tokyo, Japan) and gadoteridol (ProHance; Eisai, Tokyo, Japan) were administered at a dose of 0.2 mmol/kg body weight.

CT protocol
This was a retrospective study employing various CT scanners as follows: 16-slice multidetector-row (MD) CT scanners (SOMATOM Sensation 16; Siemens Healthineers AG, Forchheim, Germany), 64-MDCT scanners (SOMATOM Perspective; Siemens Healthineers, Forchheim, Germany) and 128-MDCT scanners (SOMATOM Definition AS+ and SOMATOM Definition Flash; Siemens Healthineers, Forchheim, Germany). The standard algorithm used a reconstruction protocol with a 5 mm slice thickness and a gapless 5 mm interval; the high-resolution algorithm used a reconstruction protocol with a slice thickness of 1 mm and a gap of 4 mm.

Evaluation of images
Musculoskeletal MRI analysis
A single radiologist with 13 years of experience in MRI interpretation and two rheumatologists with 26 and 9 years of clinical rheumatology experience, respectively,
interpreted the images independently. They were blinded to the clinical information and the presence or absence of the following features was assessed at nine sites of proximal muscles: right deltoids, R-Del; right biceps, R-BB; right triceps, R-TB; left deltoids, L-Del; left biceps, L-BB; left triceps, L-TB; left and right anterior thigh muscles (rectus femoris, vastus medialis, vastus lateralis, vastus intermedius), A-TM; left and right medial and posterior thigh muscles (adductor magnus, adductor longus, gracilis, sartorius biceps femoris, semitendinosus, semimembranosus), MP-TM; and left and right gluteus maximus, Gmax. The presence of high signal on STIR or FS Gd-T1WI was assessed. ‘Fascial pattern’ was defined as the presence of high signals in the fascia and/or in the margins of the muscles in contact with the fascia (figure 1, arrow). ‘Intramuscular pattern’ was described as the presence of high signals in the muscle away from the fascia (figure 1, arrowhead). High signals lacking fascial lesions and spreading from within the muscle were classified as ‘intramuscular patterns’, including lesions that reached the margins of the muscles. The muscle-tendon junction adjacent to the muscle insertion was excluded from the evaluation zone owing to the difficulty in distinguishing the fascial from intramuscular patterns in these areas. The images were classified as follows: ‘F’ for fascial pattern, ‘I’ for intramuscular, ‘FI’ for both fascial and intramuscular patterns, and ‘−’ for no fascial or intramuscular patterns observed (figure 1). After each observer independently evaluated the images, the three observers reviewed all images to reach a consensus. The inter-observer agreement was expressed using Fleiss’s kappa coefficient.

**Figure 1** Classification criteria for MRI findings. Representative example of ‘fascial pattern’ and ‘intramuscular pattern’ in STIR sequence. The arrow indicates a high signal in the fascia or the margins of the muscles in contact with the fascia. The arrowhead indicates a strong signal in the muscle, away from the fascia. STIR, short-tau inversion recovery.

Chest CT analysis

A radiologist with 15 years of clinical radiology experience and a rheumatologist with 9 years of clinical rheumatology experience reviewed the thin-section CT images independently, while blinded to the clinical information. According to previous reports,16 the presence of three components, ground glass opacity, consolidation and reticulation, was assessed to identify lung lesions related to anti-MDA5 antibody-positive DM. The bilateral lungs were divided into six lung zones according to their anatomical structure: the left upper divisions, left lower lobe, right upper lobe, right middle lobe and right lower lobe. Each of the six lung zones was assessed for the degree of involvement of the three components and classified as: none (0%), minimal (1%–25%), mild (26%–50%), moderate (51%–75%) or severe (76%–100%). The zone scores were as follows: no involvement=0, minimal involvement=1, mild involvement=2, moderate involvement=3 or severe involvement=4. The ‘chest CT score’ was calculated by summing the scores of the six lung zones and averaging them between two raters (range of possible scores: 0–24; online supplemental figure S1). The inter-rater reliability was assessed using the intraclass correlation coefficient.

**Histological analysis**

Muscle biopsy was performed using the en bloc biopsy method.11 Briefly, the skin, subcutaneous tissue, fascia and muscle were resected to obtain a biopsy specimen of approximately 2 cm. The obtained samples were fixed with 10% neutral-buffered formalin and embedded in paraffin. Paraffin-embedded sections of 3µm thickness were stained with H&E.

**Statistical analyses**

All statistical analyses were performed using R (R Foundation for Statistical Computing, Vienna, Austria, V.4.22) or EZR (Saitama Medical Centre, Jichi Medical University, Saitama, Japan), a graphical user interface for R.18 The Mann-Whitney U test was used to compare the mean ranks of two groups. Correlation analysis was performed using Spearman’s rank correlation test. Fisher’s exact test was employed to compare frequencies and the interobserver reliability for categorical variables was measured using Fleiss’s kappa coefficient. The strength of agreement for the kappa statistics was interpreted based on the standards proposed by Landis and Koch.19 The interpretations were as follows: <0.00, poor; 0.00–0.20, slight; 0.21–0.40, fair; 0.41–0.60, moderate; 0.61–0.80, substantial and 0.81–1.00, almost perfect. The interobserver reliability of quantitative variables was assessed using the intraclass correlation coefficient. Values of p<0.05 indicate statistical significance.

**RESULTS**

**Patients**

A total of 171 patients were diagnosed with either ‘probable’ or definite PM or DM according to the Bohan and...
Peter criteria’ or ‘probable or definite IIM based on the 2017 EULAR/ACR classification criteria’. Among them, anti-MDA5 antibody measurement was conducted in 99 patients, of whom 33 tested positive. Four patients were excluded from the study owing to the absence of MRI scans of the proximal limb muscles, and one patient was excluded as the MRI was performed more than 10 days after the initial treatment. Consequently, a total of 28 patients (20 women and 8 men) were enrolled in this study (online supplemental figure S2). These 28 patients fulfilled the criteria for definite IIM, specifically DM or ADM, according to the 2017 EULAR/ACR classification criteria.

Out of these patients, 26 (92.9%) had ILD. Fifteen patients (53.6%) were diagnosed with DM and 13 (46.4%) were diagnosed with ADM. Four of the 28 patients died within 6 months of RP-ILD, of whom 2 had ADM and 2 had DM. The serum CK levels did not differ significantly between the DM and ADM groups, whereas the serum aldolase levels were significantly higher in the DM patients (p=0.006, table 1).

### Interobserver agreement in the interpretation of musculoskeletal MRI findings

To examine the objectivity and reproducibility of the MRI evaluation method, three observers evaluated the presence or absence of the ‘fascial pattern’ and/or ‘intramuscular pattern.’ Table 2 shows the degree of concordance between the three observers at the nine muscle sites, calculated using Fleiss’s kappa coefficient. Interobserver agreement was at least moderate (kappa>0.41) in all nine sites and substantial (kappa=0.644) overall.

### Table 1 Clinical features of the 28 patients

<table>
<thead>
<tr>
<th></th>
<th>Total (n=28)</th>
<th>DM (n=15)</th>
<th>ADM (n=13)</th>
<th>P Value</th>
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<tr>
<td>Age (years)</td>
<td>55 (42.25; 63.25)</td>
<td>54 (43; 66.5)</td>
<td>56 (43; 61)</td>
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<td>Woman, n (%)</td>
<td>20 (71.4)</td>
<td>13 (86.7)</td>
<td>7 (53.8)</td>
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<td>ILD, n (%)</td>
<td>26 (92.9)</td>
<td>13 (86.7)</td>
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<td>Myalgia, n (%)</td>
<td>13 (46.4)</td>
<td>6 (40.0)</td>
<td>7 (53.8)</td>
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<td>Triple therapy, n (%)</td>
<td>20 (71.4)</td>
<td>9 (60.0)</td>
<td>11 (84.6)</td>
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<td>6-month survival rate, n (%)</td>
<td>24 (85.7)</td>
<td>13 (86.7)</td>
<td>11 (84.6)</td>
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<td>Risk score</td>
<td>0.5 (0; 1)</td>
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<td>0 (0; 1)</td>
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Laboratory tests

<table>
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<th>DM (n=15)</th>
<th>ADM (n=13)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WCC</td>
<td>4600 (3600; 5200)</td>
<td>4500 (3600; 5050)</td>
<td>4700 (4000; 5200)</td>
<td>0.503</td>
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<tr>
<td>CRP</td>
<td>0.425 (0.1275; 1.26)</td>
<td>0.51 (0.235; 1.23)</td>
<td>0.14 (0.07; 1.41)</td>
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<td>AST (U/L)</td>
<td>70 (47.25; 142.5)</td>
<td>75 (63.5; 195.5)</td>
<td>64 (36; 86)</td>
<td>0.222</td>
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<tr>
<td>ALT (U/L)</td>
<td>46.5 (27.5; 106.75)</td>
<td>47 (39; 145.5)</td>
<td>45 (26; 79)</td>
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<td>LDH (U/L)</td>
<td>385.5 (289.5; 523)</td>
<td>466 (361.5; 538.5)</td>
<td>295 (259; 498)</td>
<td>0.098</td>
</tr>
<tr>
<td>CK (U/L)</td>
<td>175.5 (61.5; 428.75)</td>
<td>240 (126.5; 475)</td>
<td>134 (41; 216)</td>
<td>0.189</td>
</tr>
<tr>
<td>ALD (U/L)</td>
<td>7.7 (5.5; 9.4)</td>
<td>8.8 (7.75; 10.7)</td>
<td>5.6 (4.7; 6.5)</td>
<td>0.006*</td>
</tr>
<tr>
<td>KL-6 (U/mL)</td>
<td>640 (420; 834)</td>
<td>626 (456.5; 1040.5)</td>
<td>654 (4.5; 769)</td>
<td>0.42</td>
</tr>
</tbody>
</table>

Data are expressed as median (first; third quartile) or percentages. The two groups were compared using the Fisher’s exact test or the Mann-Whitney U test.

*p<0.05.

ADM, amyopathic dermatomyositis; ALD, aldolase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CK, creatine kinase; CRP, C reactive protein; DM, dermatomyositis; ILD, interstitial lung disease; KL-6, Krebs von den Lungen-6; LDH, lactate dehydrogenase; WCC, white cell count.

### Table 2 Interobserver agreement in the interpretation of musculoskeletal MRI findings

<table>
<thead>
<tr>
<th>Right upper arm</th>
<th>Left upper arm</th>
<th>Femur</th>
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<tbody>
<tr>
<td>R-Del</td>
<td>R-BB</td>
<td>R-TB</td>
</tr>
<tr>
<td>0.515</td>
<td>0.61</td>
<td>0.756</td>
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</table>

Total 0.644

Fleiss’s kappa coefficients between three observers.

A-TM, anterior thigh muscles; Gmax, gluteus maximus; L-BB, left biceps brachii; L-Del, left deltoid; L-TB, left triceps brachii; MP-TM, medial and posterior thigh muscles; R-BB, right biceps brachii; R-Del, right deltoid; R-TB, right triceps brachii.
Musculoskeletal MRI finding in anti-MDA5 antibody-positive DM

Figure 2A demonstrates the musculoskeletal MRI findings of the nine sites in 28 patients, which are expressed using a colour scale. Muscles that were not imaged were labelled NA (not applicable). Each finding is represented by the colour shown in the upper right. The horizontal axis indicates the nine sites, and the vertical axis indicates the 28 patients in descending order of the number of ‘FI’, ‘I’, ‘F’ and ‘-’ patterns.

Nine patients (32.1%) had ‘FI’ patterns in at least one of the sites (patient nos 1–9), six (21.4%) had only ‘I’ patterns (patients nos 10–15), seven (25%) had only ‘F’ patterns (patients nos 16–22) and six (21.4%) had no increased signal in the evaluation range (patients nos 23–28).

Figure 2B summarises the percentage of ‘FI’, ‘I’, ‘F’ and ‘-’ on each site. The rate of ‘-’ was the highest on all sites. ‘I’ patterns were observed on all sites except the R-BB.

Muscle biopsies were conducted in 7 out of 28 patients. Online supplemental figure S3 displays a representative example of MR and pathology images for patient no. 9 (R-TB), classified as ‘FI’ in musculoskeletal MRI (STIR sequence). Subsequently, en bloc biopsy was performed and perivascular inflammatory cell infiltrations were observed at the fascia layer and their adjacent muscular layer. This corresponded to a high signal intensity of the fascia on MRI that we classified as ‘Fascial pattern.’ However, the intramuscular signal (arrowhead) could not be pathologically evaluated.

We defined patients presenting with intramuscular patterns in any of the nine sites as positive for ‘radiological myositis.’ Additionally, we used the ‘myopathic proportion’, a scoring system designed to assess the extent of muscle involvement in the nine sites of proximal muscles by considering the distribution of intramuscular lesions observed in MRI. The myopathic proportion is calculated as the proportion of sites presenting with intramuscular patterns above the imaged sites (ie, the number of (FI+I)/(9−NA)).

Patients with ‘radiological myositis’ (myopathic proportion >0) were classified into the radiologically myopathic DM (RMDM, n=15) group. Those without intramuscular patterns in any region (myopathic proportion=0) were classified into the radiologically amyopathic DM (RADM, n=13) group (figure 2A).

Relation between intramuscular lesions and muscle symptoms

To determine whether intramuscular lesions were related to muscle-associated symptoms and laboratory findings, we examined the relationship between the myopathic proportion and muscle symptoms (figure 3A), and the correlation between the myopathic proportion and serum creatine kinase (CK) levels (figure 3B). The myopathic proportion in patients with DM (with muscle weakness) was higher than that in patients with ADM (without muscle weakness); however, the difference was not significant (median: 0.22 vs 0; p=0.0574). In patients with ADM, despite the absence of muscle weakness, 5 out of 13 patients were classified in the RMDM group with a myopathic proportion greater than 0 (figure 3A).
Among these patients, myalgia was observed in the top four individuals with a high myopathic proportion. Conversely, among the eight patients classified as having RADM in ADM patients, only three had myalgia. Additionally, among the 15 patients with DM, 5 had a myopathic proportion of 0 and were classified into the RADM group. No significant correlation was found between the myopathic proportion and serum CK levels ($\rho =0.279$, $p=0.151$).

Patient characteristics in the RMDM and RADM groups
Table 3 shows patient characteristics and a comparison between the RMDM and RADM groups. Based on the reported high mortality rate within 6 months for RP-ILD associated with anti-MDA5 antibody-positive DM, we compared the survival rates of the two groups at 6 months from diagnosis. None of the RMDM patients died within 6 months, whereas 4 of the 13 patients in the RADM group died within 6 months. The 6-month survival rate was significantly higher in the RMDM group than in the RADM group (100% vs 69.2%; $p=0.035$). The log-rank test also confirmed that the survival rate of the RADM group was significantly lower within 6 months ($p=0.022$, figure 4). Significantly fewer patients in the RMDM group than in the RADM group were treated with the triple therapy of prednisolone, calcineurin inhibitors and cyclophosphamide (53.3% vs 92.3%; $p=0.038$). The risk scores, calculated from serum CRP and KL-6 levels (CRP$\geq0.8$mg/dL and KL-6$\geq1000$U/mL), were lower in the RMDM than in the RADM groups, although the difference was not significant (median: 0 vs 1; $p=0.251$). In laboratory tests, the white cell count was significantly lower in the RMDM group than in the RADM group ($p=0.021$).

Relation between intramuscular lesions and chest CT images
We compared the spread of lung lesions at the time of diagnosis using the chest CT scores (figure 5). The chest CT score was calculated by averaging the scores provided by two raters. The intraclass correlation coefficient was determined to be 0.936 (95% CIs 0.868 to 0.970), indicating a high level of reliability. The scores were significantly higher in the RADM group than in the RMDM group ($p=0.023$). The scores were widely distributed from low-to-high in the four death cases (figure 5A, arrowhead). The chest CT score negatively and significantly correlated with the myopathic proportion ($p=-0.547$, $p=0.003$, figure 5B). Further analysis of the correlation between the myopathic proportion and chest CT score, specifically for the upper arm ($p=-0.68$, $p=0.0001$) and femur ($p=-0.349$, $p=0.0948$), revealed a stronger negative correlation in the upper arm (figure 5C).

DISCUSSION
In this study, we explored a novel musculoskeletal MRI evaluation method and found three important clinical observations. First, intramuscular lesions were detected in more than half of the patients with anti-MDA5 antibody-positive DM, including ADM, which was an unexpectedly high percentage. Second, patients with radiological myositis had a higher survival rate than those without radiological myositis, despite a lower rate of triple therapy for anti-MDA5 antibody-positive DM. Third, patients with a higher proportion of intramuscular lesions on MRI had fewer extensive lung lesions.

This study is the first to report the characteristics, distribution and frequency of muscle lesions on MRI findings in patients with anti-MDA5 antibody-positive DM. Our novel method, which evaluates MRI signals
Myositis separately at the fascia and intramuscularly in the proximal limb muscles, is convenient and highly reproducible. Anti-MDA5 antibody-positive DM is associated with fewer muscle symptoms. However, more than 75% of the patients had fascial or intramuscular lesions on MRI, and more than half of the patients had intramuscular lesions, which were defined as ‘radiological myositis’. Our findings assume importance because musculoskeletal MRI provides new information regarding the pathophysiology of anti-MDA5 antibody-positive DM. Interestingly, the degree of intramuscular lesions on MRI did not correlate with serum CK levels and was observed even in patients with ADM (figure 3). These data suggest that serum CK levels and clinical symptoms were not predictive of radiological myositis in patients positive for anti-MDA5 antibodies. The significance of musculoskeletal MRI signals in anti-MDA5 antibody-positive DM could be estimated through pathological analysis. Pathological analysis of the area corresponding to the fascial pattern showed perivascular inflammatory cell infiltration in the fascial and adjacent muscular layers (online supplemental figure S3), which is consistent with a previous report that perivascular inflammatory cell infiltration is occasionally observed, although it is not a specific feature of anti-MDA5 antibody-positive DM. Meanwhile, the

### Table 3 Patients’ characteristics in the RMDM and RADM groups

<table>
<thead>
<tr>
<th></th>
<th>RMDM (n=15)</th>
<th>RADM (n=13)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>46 (32.5; 58)</td>
<td>61 (56; 64)</td>
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<tr>
<td>Woman, n (%)</td>
<td>11 (73.3)</td>
<td>9 (69.2)</td>
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<td>ILD, n (%)</td>
<td>13 (86.7)</td>
<td>13 (100)</td>
<td>0.484</td>
</tr>
<tr>
<td>Myalgia, n (%)</td>
<td>9 (60.0)</td>
<td>4 (30.8)</td>
<td>0.151</td>
</tr>
<tr>
<td>Subtypes, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DM</td>
<td>10 (66.7)</td>
<td>5 (38.5)</td>
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</tr>
<tr>
<td>ADM</td>
<td>5 (33.3)</td>
<td>8 (61.5)</td>
<td>0.255</td>
</tr>
<tr>
<td>Triple therapy, n (%)</td>
<td>8 (53.3)</td>
<td>12 (92.3)</td>
<td>0.038*</td>
</tr>
<tr>
<td>6-month survival rate, n (%)</td>
<td>15 (100)</td>
<td>9 (69.2)</td>
<td>0.035*</td>
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<tr>
<td>Risk score</td>
<td>0 (0; 1)</td>
<td>1 (0; 1)</td>
<td>0.251</td>
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<tr>
<td>Laboratory tests</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WCC</td>
<td>3600 (3300; 4850)</td>
<td>4800 (4400; 6000)</td>
<td>0.021*</td>
</tr>
<tr>
<td>CRP</td>
<td>0.24 (0.13; 1.23)</td>
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<td>AST (U/L)</td>
<td>64 (45.5; 195.5)</td>
<td>72 (64; 86)</td>
<td>0.836</td>
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<tr>
<td>ALT (U/L)</td>
<td>46 (25.5; 163)</td>
<td>49 (39; 79)</td>
<td>1.000</td>
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<tr>
<td>LDH (U/L)</td>
<td>378 (294.5; 555)</td>
<td>387 (276; 498)</td>
<td>0.717</td>
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<td>CK (IU/L)</td>
<td>261 (80; 475)</td>
<td>161 (41; 216)</td>
<td>0.289</td>
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<tr>
<td>ALD (IU/L)</td>
<td>8.1 (5.95; 10)</td>
<td>6.5 (4.9; 8.8)</td>
<td>0.345</td>
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<tr>
<td>KL-6 (U/mL)</td>
<td>599 (366; 783)</td>
<td>657 (488; 972)</td>
<td>0.345</td>
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</table>

Data are expressed as median (first; third quartile) or percentages. The two groups were compared using the Fisher’s exact test or the Mann-Whitney U test.

*p<0.05.

ADM, amyopathic dermatomyositis; ALD, aldolase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CK, creatine kinase; CRP, C reactive protein; DM, dermatomyositis; ILD, interstitial lung disease; KL-6, Krebs von den Lungen-6; LDH, lactate dehydrogenase; RADM, radiologically amyopathic dermatomyositis; RMDM, radiologically myopathic dermatomyositis; WCC, white cell count.
pathological condition of the intramuscular pattern is ambiguous because deep intramuscular lesions are not usually excised via en bloc biopsy. As the degree of intramuscular lesion has a low correlation with serum CK levels, the ‘intramuscular pattern’ may not solely reflect the destruction or inflammation of the muscle fibres. Rather, it may also reflect vasculopathy, which is proposed as a hypothesis for vasculopathy in anti-MDA5 antibody-positive DM.21 This finding is consistent with a previous study that identified skin ulcers and myasthenia as characteristic features within the same group.5 In the RMDM group of this study, there were five patients with ADM with confirmed intramuscular lesions on MRI, although muscle weakness was not observed. This finding implies that in cases where inflammation predominantly occurs around the blood vessels surrounding the interstitial spaces between muscle fibre bundles, muscle weakness may not be detected by MMT, even if intramuscular lesions are visible on MRI. Although not statistically significant, ADM patients with intramuscular lesions on MRI had a higher frequency of myalgia than to those without such lesions. This finding indicates a possible association between intramuscular lesions on MRI and the development of myalgia. Further analysis is necessary to gain a better understanding of the significance of these MRI lesions in ADM.

Patients with radiological myositis had higher survival rates than those without radiological myositis, despite a lower rate of triple therapy for anti-MDA5 antibody-positive DM. This finding suggests that the presence of intramuscular lesions on MRI may predict the prognosis of ILD. Our study proposes that the classical concept of ‘the ILD may exacerbate in patients with clinically ADM’ may be replaced with ‘the ILD may exacerbate in patients with radiologically ADM.’ Both ADM and DM were included in the fatal cases, and the chest CT scores were not necessarily high. Therefore, the presence of an intramuscular lesion predicted a favourable prognosis rather than the spread of the lung lesion or muscle symptoms, indicating the significance of musculoskeletal MRI at diagnosis. Although poor prognostic factors are known, favourable prognostic factors based on positive findings have rarely been reported. A previous study reported that myofas-cia-dominant involvement in whole-body MRI is a risk factor for RP-ILD in patients with inflammatory muscle disease.22 MRI findings with myofascial dominance indicate relatively few intramuscular lesions. Consistent with these findings, the results from this study showed a worse prognosis in the RADM group with no intramuscular lesions. While the report by Karino et al included patients with DM who had different types of antibodies, including 13 patients with anti-MDA5-positive DM, our study recruited a larger sample size (n=28) with anti-MDA5-positive DM. Although the evaluation method of this study had poor quantitative performance compared with whole-body MRI, it has the advantage of including an evaluation using standard MRI, which is widely used worldwide, using a simple and reproducible assessment method. More patients in the RMDM group were treated without cyclophosphamide but with prednisolone and calcineurin inhibitors. The observation that the RMDM group had less extensive lung involvement compared with the RADM group suggests that the treatment choice may have been influenced by the clinical severity of respiratory involvement. Still, despite this difference in treatment, the survival rate was higher in this patient group, suggesting that excessive immunosuppression can be avoided in patients with RMDM.

Patients with a higher proportion of intramuscular lesions had fewer extensive lung lesions than those with a lower proportion of intramuscular lesions. Notably, a stronger negative correlation was observed in the upper arm and femur. *p<0.05, using the Spearman’s rank correlation analysis. Among the 28 patients, 2 were excluded from the analysis due to the absence of upper arm MRI, and 4 were excluded due to the absence of femur MRI. RADM, radiologically amyopathic dermatomyositis; RMDM, radiologically myopathic dermatomyositis.
arm compared with the femur. The weaker correlation observed in the femur can be attributed to previous reports indicating that exercise load can induce changes in signal intensity on STIR sequences in MRI scans of patients with juvenile IIM.\textsuperscript{23} This suggests that the femur, being subjected to gravitational load, may exhibit signals that are unrelated to muscle inflammation. Therefore, it is possible that the upper arm is a more suitable site for evaluating intramuscular lesions in MRI scans. Though lung and intramuscular lesions were conflicting at the time of diagnosis, we observed that patients presenting with radiological myositis, including those with extensive lung lesions at diagnosis, had better survival rates. Further research is needed to understand the relationship between the lungs and proximal muscles. It is possible that the aforementioned clinical phenotypes may be involved, as the group with higher proximal muscle weakness had less RP-ILD and a lower death rate.\textsuperscript{3}

This study had three limitations. First, the images of all nine sites were not obtained for all patients; thus, we cannot exclude the presence of other findings in sites that were not imaged. Therefore, the RADM group may have included patients with a favourable clinical course. In most situations, not all sites could be imaged in clinical practice; despite this, an intramuscular lesion at a single site may be a sign of favourable prognosis. Second, there was a bias because of the absence of MRI in patients with extremely poor respiratory status. Therefore, the intramuscular signal on MRI is only useful for predicting the future course of patients whose respiratory status is maintained at the time of diagnosis. However, among the 28 patients, 15 (53.6\%) were diagnosed with muscle weakness in DM, which is generally consistent with the reported prevalence of DM with muscle weakness in Japanese patients with anti-MDA5 antibody-negative DM (48\%–66.7\%).\textsuperscript{2,24} Thus, it can be inferred that the cohort was not biased towards either DM or ADM. Third, while our findings suggest a favourable prognosis for the RMDM group, the absence of fatalities in this group may be due to the limited sample size. To further investigate the impact of intramuscular lesions on prognosis in the RMDM group, a larger and more diverse sample size should be included in future studies.

In conclusion, we demonstrated that patients with radiological myositis had higher survival rates in anti-MDA5 antibody-positive DM. The detection of intramuscular lesions on musculoskeletal MRI using our novel evaluation method may be clinically useful as a favourable prognostic marker. Thus, including MRI in the initial examination of patients with anti-MDA5 antibody-positive DM may provide guidance for selecting treatment strategies.

**Acknowledgements**  The authors thank Dr Masataka Kuwana (Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan) for his help with the detection of anti-MDA5 antibodies. The authors also thank Dr Tsukasa Kadota and Dr Mina Gochi (Division of Respiratory Diseases, Department of Internal Medicine, The Jikei University School of Medicine, Kashiwa Hospital) for their help with medical support.

**Contributors**  YO and KY contributed equally to this study. YO was responsible for the study design, data acquisition, analysis and interpretation, reading of MR images and CT images, drafting and critical revision of the article. KY was involved in the study design, reading of MR images, data acquisition and interpretation, and drafting and critical revision of the manuscript. TF contributed by reading MR images, interpreting data and providing critical revisions to the manuscript, while TF was responsible for reading CT images and interpreting data. TU performed data acquisition and revision of the manuscript. KN contributed to data acquisition and revision of the article, HI contributed to data acquisition and interpretation, and DK provided data interpretation and critical revisions to the article. YO is the author responsible for the overall content as guarantor. All the authors have read and approved the final manuscript.

**Funding**  The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests**  None declared.

**Patient consent for publication**  Not applicable.

**Provenance and peer review**  Not commissioned; externally peer reviewed.

**Data availability statement**  Data are available on reasonable request.

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